Seminar, Cornell University, March 16, 1971

EXPANDING CONCEPTS IN GENETICS.

I. INTRODUCTION.

1. Periods in genetics, changes in concepts: Mendelian inheritance, genes and chromosomes; period of cytogenetics; beginnings of biochemical genetics; microbiology + molecular biology, bacteria and phage.

Present: period of transition; from microorganisms to eukaryotic organisms. Reassesment of concepts based on increased knowledge of eukaryotic organisms, degrees of complexity, failures of some concepts from microbiology when applied to higher organisms. Euphoria of early sixties gone: evening at Demerec home, 1963 symposium. Effect: Gunther Stent, Bentley Glass: all is over with respect to principles.

2. Prediction: Studies of eukaryotic organisms, from all points-of-view will produce very great change in concepts regarding: nature of "mutations" nature of evolutionary processes; the nature of programming mechanisms during development; the nature of homeostatic mechanisms; the vast amount of symbiosis at all levels of organization-- the oneness of nature in general.

3. The legacy from microbial-molecular biology:

The Central Dogma: DNA-RNA-Protein (Already broken down.)

Organization of DNA: operons, cistrons, operator, regulators, DNA of stop and start signals;

Reading of DNA: Strands and directions, linear.

Ribosomes, transfer RNA, ribosomal RNA,

Replicons; Membranes; sites on membranes;

Repair mechanisms; exchange mechanisms; ligases; nucleases

Mutations from base changes; Supressors and tRNAs

Transformation; transductios; lysogeny; plasmids;

Self-assembly mechanisms.

4. Control systems: Complex, even in the microorganisms. Far more complex in the eukaryotic organisms. Regardless, legacy from molecular biology of microorganisms is vast and directing.

5. Eukaryotic organisms: Mechanisms discovered in microorganisms apply but other integrating mechanisms ~~kinds~~ expand and confound the experimental proceedures aiming at direct comparisons.

Eukaryotic organisms: DNA is subject to large amounts of manipulation in many organisms. Increases, decreases, transpositions, various types of organizations and reorganizations. Nearly any type or manipulation imagined could probably be found to occur in some organism.

Organisms with greatest breadth of experimentation -- not the vertebrates, they are relatively dull. Should look to the invertebrates for examples of vastly different types of manipulation: Protozoans, insects, known to have many changes during development.

The vertebrates: Many interesting types of manipulation of genome; that occurring in one group usually applies to other groups.

Plants: Less gross manipulations of genome; programming less tight. Range in products made= extraordinary in kinds produced. Interrelationship with other organisms:symbiosis at a distance in flower patterns, some products made by plants.

II. THE EFFECT OF RECENT INVESTIGATIONS ON CONCEPTS: A LIST (only)

1. The composition of DNA in eukaryotic organisms: Repetitious DNA; satellite DNAs, total amount of DNA and relation to repetitious DNA; rDNA, tDNA.

2. Inconstancy of DNA composition in different types of cells: Increases and decreases of parts of genome, from small to large components.

3. Types of metabolic DNA: derived from parts of the genome.

4. Homeostatic mechanisms arrangeing amounts and locations of DNA within cells.

5. Different ways that eukaryotic organisms solve one kind of problem.

6. Symbiotic relationships involving DNAs of different origins.

7. The nature of programming mechanisms: sequences of "determination" events in development.

8. MOST IMPORTANT: Recognition of constitution of eukaryotic cells: Mitochondria, chloroplasts; organization of cilia, flagella, centrioles; microtubules; origins of membranes; organization of components of chromosomes: replicons; rings; nature of true heterochromatin;

Eukaryotic cell: made up of a number of different parts that initially were much alike: Symbiotic soup.

9. Tempted to consider evolution by consolidation of individual components. Must consider possibility of origin of some individual components--bacteria; phage; viruses--as escapes from more complex organizations. At present time, viruses are posing this problem in a most definite manner. We may find more instances for reco sidering evolutionary mechanisms -- away from the single mechanism of base pair changes.

III. SOME EXAMPLES OF SYMBIOSIS AT THE LEVEL OF DNA.

1. Bacteria: lysogeny; plasmids. 3) Virus - DNA + RNA-DNA.

2. Bacteria: transductions; transformations; significance. Attempts with eukaryotic organisms: Mostly negative in early studies. Szbalski, Nawa and Caspari; Fox.

3. Brussels meeting; late August, early September: INCORPORATION OF INFORMATIONAL MACROMOLECULES. Ledouc with bacteria and plants, sponsor. Results of symposium:

(2) see card

(1)

→ incorporation of metaphase chromosomes - Results

(3) Chicken erythrocyte / HeLa cell - genetic Test - Results.

(4) B-The chromosomes.

3. Time for conference ripe: reason, the studies of animal viruses in tissue cultures.

DNA viruses into chromosomes; transformation event.

RNA viruses - DNA - (into chromosomes?)

Coats of RNA viruses: part of membrane of cell, slightly altered.

Are viruses escaped DNA using sites on membranes for coats?
Do they introduce DNA from one organism to another?
Are they present in nuclei of most if not all eukaryotic organisms?
Hubner - Todaro hypothesis; Dept. of Embryology addition to th

IV. THE STRANGE CASE OF SATELLITE DNAs.

1. The composition of DNAs. Differences seen at pachytene stage of meiosis:
Organization types: SLIDES

2. The distribution of "heterochromatin": Species of Nicotiana:
staining properties - fluorescence - compactness differences along chr; Regions
The races of maize: no knobs, knobs, sizes, content of knobs; metabolic DNAs. SLIDES

3. Satellite DNA: Initial case, Mouse DNA. SLIDE 10
Location of satellite DNA: Adjacent to centromere regions. Slide 11
Repetitious DNA and Satellite DNA - relation of mouse to rat.
Unique presence of mouse Satellite DNA.

4. Other satellite DNAs: Walker, etc.
(1) Species restricted
(2) genera distributed - AT-AT Type Crabs

5. Most extraordinary study of satellite DNA and distributions: Related species Sat DNA's ~DNA
Drosophila hydei; neohydei, pseudoneohydei.
Tests of satellite DNAs: making RNA from different isolates; annealing with salivary gland chromosomes; locations of satellite DNAs found.
The relation of Dros. neohydei to pseudoneohydei. Slides 12 To 15
The significance of this knowledge: Incorporation of unique sequences of DNA and their transpositions to various locations. What is origin of these unique sequences? Foreign?

6. The distributions of A-T-A-T satellite DNAs among crab genera and species: Relation to knobs and races of maize?

7. The problem: Are there classes of satellite DNAs? Do they have different origins? Can many of them represent symbiotic conditions initially? Not impossible: the intranuclear bacteria in Paramoecium SLIDE.

Parasites within parasites: Preer. Slide

8. The conclusion: GENERAL FLOW OF GENETIC INFORMATION FROM ONE ORGANISM TO ANOTHER. COULD RESULT IN MARKED CHANGES IN DNA CONTENT AND ACTIONS IF INCLUSIONS AND REPLACEMENTS WERE COMPATIBLE.

V. HOMEOSTATIC MECHANISMS INVOLVING COMPONENTS OF DNA: EXAMPLE, rDNA.

1, Oocytes of Xenopus, Triturus; multiple nucleoli; released from nucleolus organizer; formation of many nucleoli = ribosomes in cytoplasm. Very much publicised. Other similar cases: insects.

2. Oocytes of Tailed Frog: 8 nuclei; similar patterns; loss of 7.

3. Oocytes: Drosophila : 16 cells, 15 murse: 1 oocyte; RNA productions.

4. Oocytes, Rhyncosciara: One oocyte; one nurse cell; DNA of nurse cell: sequence of events:

5. The nucleolus organizer: Maize and Chironomous: Multiple; control of amount of action: multiple "operators" but control of which is active; Types in maize: SLIDE

6. Nucleolus organizer in Drosophila: Suggests only one operator. Extraordinary homeostatic events:

Bobbed cases:

XX, XY, XO - XX. Change in rDNA cistrons with controls.

b. Nucleolus organizers: birds; microchromosomes: SLIDE

VI. HOMEOSTATIC MECHANISMS INVOLVING COMPONENTS OF DNA: Replicon increases,

1. Specific bands in salivary gland chromosomes of Chironomous: Continuous DNA replication and release, as no accumulation.

2. Specific bands in Sciara group, Chironomous as seen in salivaries:

1 - 2 - 4 - 8 - 16. Not released but continuous in chromosome.

3. Relation of this mechanism to evolution of some families:
Ranunculacele: Metaphase chromosomes: SLIDE
DNA content: 1 - 2 - 4 - 8 - 16 Ris and Kubai.

VII. HOMEOSTATIC MECHANISMS INVOLVING LOSSES OF DNA: Heterochromatin losses: Soma vs germ line:

1. Ascaris; Copepods; elimination of heterochromatin.

2. Extreme cases: Elimination chromosomes in Cecidomyids:

   Zygote: 4 + 4 soma chromosomes + 30 or more Elimination chromosomes

   Germline, retains E chromosomes; soma loses all E chromosoes.

   Action of E chromosoes: take over functions of organizing the gonads and germ cells. Soma chromosomes appear to be inactive. Fantastic controls evident by organization and behavior of two types of chromosomes in development of oocyte.

   Illustrate extreme case of separation of programming of chromosome sets.

VIII. THE SIGNIFICANCE OF TRUE HETEROCHROMATIN. satellite DNAs

IX. CONCLUSIONS: New concepts must incorporate knowledge of:

1. Symbiosis: related to organizations in past evolution produces exchanges between genomes at all levels of organizations.

2. Manipulations of DNA: part of the developmental and the evolutionary events responsible for action of present day organisms. All types of manipulation known among different groups of organisms. Only a few cases could be mentioned here: Others extraordinary: "acronuclear anlaga of some protozoans. Controlled non-disjunctions; Controlled transpositions; Various aspects of "metabolic DNA". Controlled endomitoses: set from one parent only; other not replicated. Many other instances of manipulation.

3. Programming of the genome: not considered in this talk, but basic changes in organization of DNA during development, involving components of gene locus: locus is large to accomodate changes. (gene)

4. Evolutionary mechanisms: much more than mutations through base-pair substitutions. Involve the above three basic actions.

5. the nature and action of true heterochromatin.

Any organism can make any other organism. Enzymes much alike; they are only the tools, putting together and taking apart where energy and speed required.

SLIDES

1. Medicargo murex (2n= 16). Pachytene, several chromosomes.
2. Salvia, pachytene stage
3. Bermuda grass " "
4. Sorghum " "
5. Tomato " "
6. Maize " "
7. " Feulgen " " B chromosome bivalent
8. Quinacrine mustard fluorescent staining. Casperson, original paper
9. Amounts of DNA per haploid complement. Table from Ris and Kubai
10. Diagram Mouse DNA. Original
11. Mouse Sat. DNA location (gross) Metaphase chromosomes. Pardue and Gall
12. H^3 synthetic main band RNA from Drosophila neohy.on denatured salivary gland chromosomes of Dros. neohydei/hydei
13. Drosophila melanogaster: ectopic pairing. Kaufmann and Iddles, 1965.
14. H^3 synthetic RNA binding to denatured salivary chrs. of Dros neohydei. from heavy satellite DNA of Dros. neohydei(Ectopic regions)
15. " " " " " " " " " of Dros. pseudoneohydei. (Pattern general; about same as with neohydei)
16. Ranunculaceae: genera. Metaphase chromosomes
17. DNA content of chromosomes from different organisms: Ris and Kubai